



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

FEB 26 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

PR Notice 88-2

Notice to Producers, Formulators, Distributors and Registrants

Attention: Person(s) Responsible for Federal Registration
of Quaternary Ammonium Compounds

Subject: Clustering of Quaternary Ammonium Compounds

This Notice announces that the United States Environmental Protection Agency ("EPA or Agency") has clustered the Quaternary Ammonium Compounds (Quats) into four (4) groups for the purpose of testing chemicals in order to build a data base that will support the continued registration of the entire family of quaternary ammonium compounds.

I. Background

In the past, EPA has required each Quat compound to be individually coded and registered as a new chemical, even when the chemical structure of individual compounds differed only slightly in alkyl distribution and chain lengths. This procedure was continued with the new generations of Quats having two, three, and four chains. As a result, EPA records show some 211 registered technical grade active ingredient products containing varying concentrations of Quats, each coded separately on the basis of alkyl chain length and percentage carbon distribution within the chain. Currently, there are approximately eight to ten thousands (8-10,000) registered end-use formulations.

In FY 1986, EPA developed and issued a registration standard for the first Quat compound, ADBAC, one of today's most widely used Quats. This Quat was chosen because it contains a single active ingredient which has a single alkyl chain; appears in a large number of registered end use products; and has use patterns that appear to be typical of the Quats. During the course of the development of the standard, questions were raised regarding whether EPA could cluster or group the Quats and pick one or more

representative members of each cluster to be used in toxicity studies, instead of requiring separate studies on each Quat. These same questions were raised when EPA issued its March 4, 1987 Data Call-In Notice requiring all registrants of antimicrobial active ingredients to submit subchronic and chronic toxicological data to support the continued registration of their products.

II. Decision

In response to these questions, EPA solicited information from industry, the public, academia, industry cooperative work groups, the state of California, and Canada. EPA then reviewed all of the assembled information along with the chemical structure of most of the Quats. Based on the results of this review, EPA developed the following four groupings of currently registered Quat compounds:

- Group I. The alkyl or hydroxyalkyl (straight chain) substituted Quats
- Group II. The non-halogenated benzyl substituted Quats (includes hydroxybenzyl, ethylbenzyl, hydroxyethylbenzyl, naphthylmethyl, dodecylbenzyl, and alkyl benzyl)
- Group III. The di- and tri- chlorobenzyl substituted
- Group IV. Quats with unusual substituents (charged heterocyclic ammonium compounds)

For Group I, EPA will allow a full set of subchronic and chronic toxicity studies on the didecyl dimethyl ammonium Quat (#69149), and a teratology study on one of the alkyl trimethyl Quats (such as #69151) to be submitted (or cited, to the extent allowed by FIFRA section 3(c)(2)(D)) in lieu of the subchronic and chronic studies on individual Quats required by the March 4, 1987, Data Call-In Notice.

For Group II, EPA will allow a full set of subchronic and chronic studies on ADBAC to be submitted (or cited, to the extent allowed by FIFRA section 3(c)(2)(D)) for the subchronic and chronic toxicity studies on each individual Quat required by the March 4, 1987 Notice. EPA notes that after evaluating the data it expects to receive on the Group I and II compounds, it may also require one or more studies using #69154, an alkyl dimethyl ethylbenzyl Quat with 68% C₁₂ and 32% C₁₄ alkyl chains, to determine whether the Group I and ADBAC data are representative of the toxicity of the ethylbenzyl Quats.

For Group III, EPA will allow a full set of subchronic and chronic studies on #069145 to be substituted for the similar studies on other members of the alkyl dimethyl 3,4-dichlorobenzyl Quats required by the March 4, 1987 Notice. Since all products in this group contain only the 3,4 dichlorobenzyl group and have very similar composition, testing one member of this group should be sufficient.

For Group IV, EPA has been unable to conclude that any small subset of Quats would be adequate testing surrogates for the other members of the Group. Thus, each chemical must be tested separately, unless registrants can develop a testing scheme using representative compounds that is acceptable to EPA.

Examples and chemical structures of each of the groups are provided in the Appendix to this PR Notice.

If you have any questions concerning this Notice, you may contact:

John H. Lee, Product Manager 31
Registration Division (TS-767C)
Office of Pesticide Programs
Environmental Protection Agency
Washington, D.C. 20460
Telephone (703) 557-3675

or

Valdis Goncarovs, same address
Telephone (703) 557-3663

Sincerely,



Edwin F. Tinsworth, Director
Registration Division (TS-767C)

Appendix

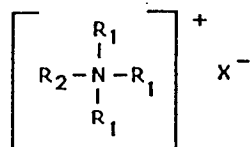
Group I

The alkyl or hydroxyalkyl (straight chain) substituted quats

Examples:

- a) alkyl dimethyl ethyl ammonium halide
- b) alkenyl dimethyl ethyl ammonium halide
- c) alkyl bis(2-hydroxyethyl) methyl ammonium halide
- d) 3-alkoxy-2-hydroxypropyl trimethyl ammonium halide

Structure:



where R_1 = methyl, ethyl, hydroxyethyl or hydroxypropyl
 $R_2 = C_nH_{2n+1}$ or C_nH_{2n} ; $n = 8 - 18$; X = any anionic species.

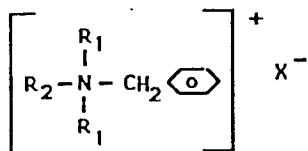
Group II

The non-halogenated benzyl substituted quats

Examples:

- a) Alkyl dimethyl 1-naphthylmethyl ammonium halide
- b) Alkyl bis(2-hydroxyethyl) benzyl ammonium halide
- c) Alkyl dimethyl ethylbenzyl ammonium cyclohexylsulfamate
- d) Alkyl dimethyl benzyl ammonium saccharinate
- e) Alkyl dodecylbenzyl dimethyl ammonium halide
- f) Alkylbenzyl trimethyl ammonium halide

Structure:



where R_1 = methyl or hydroxyethyl
 $R_2 = C_nH_{2n+1}$, $n = 8 - 18$, predominantly 12, 14, or 16
 X = any anionic species.

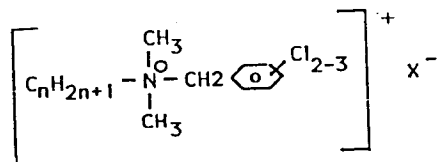
Group III

The di- and tri- chlorobenzyl substituted quats

Examples:

- a) Alkyl * dimethyl 3,4-dichlorobenzyl ammonium chloride
 *(90% C₁₄, 5% C₁₆, 5% C₁₂)

Structure:

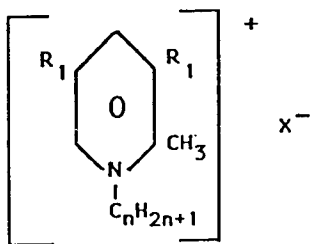


$$n = 12 - 18$$

Group IV

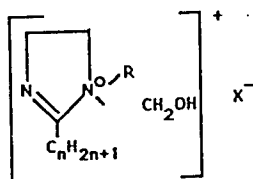
Those with unusual substituents (charged heterocyclic ammonium compounds)

- a) Picolinium



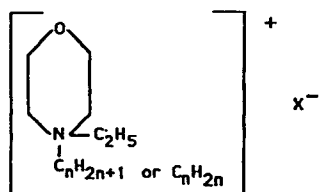
$$\begin{aligned} \text{R}_1 &= \text{C}_2\text{H}_5 \text{ or } \text{H} \\ n &= 12-16 \end{aligned}$$

- b) Imidazolinium



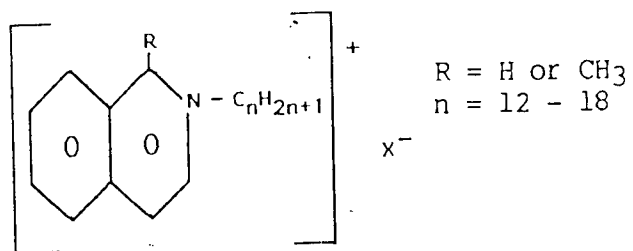
$$\begin{aligned} \text{R} &= \text{H}, \\ \text{R} &= -\text{CH}_2 - \text{C}_6\text{H}_4, \\ \text{R} &= -\text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{CH}_2 - \text{Cl} \\ n &= \text{C}_8 - \text{C}_{18} \end{aligned}$$

- c) N-Ethyl-Morpholinium



$$n = 14 - 18$$

d) Isoquinolinium



e) Alkyl 5-hydroxy-4-oxo-2(4H)-pyranylmethyl dimethyl ammonium chloride

